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# Ambient air pollution as a risk factor for lung cancer

Aaron J. Cohen, D.Sc.,<sup>(1)</sup> C. Arden Pope, III, Ph.D.,<sup>(2)</sup> Frank E. Speizer, M.D.<sup>(3)</sup>

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## Abstract

Epidemiologic studies over the last 40 years have observed that general ambient air pollution, chiefly due to the by-products of the incomplete combustion of fossil fuels, is associated with small relative increases in lung cancer. The evidence derives from studies of lung cancer trends, studies of occupational groups, comparisons of urban and rural populations, and case-control and cohort studies using diverse exposure metrics. Recent prospective cohort studies observed 30-50% increases in the risk of lung cancer in relation to approximately a doubling of respirable particle exposure. While these data reflect the effects of exposures in past decades, and despite some progress in reducing air pollution, large numbers of people in the US continue to be exposed to pollutant mixtures containing known or suspected carcinogens. These observations suggest that the most widely cited estimates of the proportional contribution of air pollution to lung cancer occurrence in the US, based largely on the results of animal experimentation, may be too low. It is important that better epidemiologic research be conducted to allow improved estimates of lung cancer risk from air pollution in the general population. The development and application of new epidemiologic methods, particularly the improved characterization of population-wide exposure to mixtures of air pollutants and the improved design of ecologic studies, could improve our ability to measure accurately the magnitude of excess cancer related to air pollution.

Key words: air pollution; lung neoplasms/risk; review

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## Resumen

En los estudios epidemiológicos llevados a cabo durante los últimos 40 años se ha observado que la contaminación del aire en general, debida sobre todo a los residuos de la combustión incompleta de combustibles fósiles, se ha asociado a pequeños incrementos relativos de cáncer pulmonar. La evidencia procede de estudios sobre tendencias de cáncer del pulmón, de aquellos sobre grupos ocupacionales, de comparaciones entre poblaciones urbanas y rurales y de estudios de casos y controles y de cohortes en los cuales se utilizaron diversas mediciones de exposición. En estudios de cohortes prospectivos realizados recientemente se observaron incrementos del 30 al 50% en el riesgo de contraer cáncer pulmonar con respecto a aproximadamente el doble de la exposición a las partículas inhalables. Si bien estos datos reflejan los efectos de las exposiciones durante décadas pasadas, y a pesar de los logros en materia de reducción de la contaminación del aire, son muchas las personas en los Estados Unidos de América (EUA) que siguen estando expuestas a las mezclas contaminantes que contienen carcinógenos conocidos o cuya existencia se sospecha. Estas observaciones sugieren que pueden ser demasiado bajas las estimaciones más ampliamente citadas de la contribución proporcional de la contaminación del aire a la ocurrencia de cáncer pulmonar en los EUA, basadas fundamentalmente en los resultados de la experimentación animal. Es importante que se lleve a cabo una mejor investigación epidemiológica para obtener estimaciones más aproximadas del riesgo de cáncer pulmonar a partir de la contaminación del aire, en la población general. El desarrollo y la aplicación de nuevos métodos epidemiológicos, particularmente el mejoramiento en la caracterización de la amplia exposición de la población a mezclas de contaminantes del aire y las modificaciones al diseño de los estudios sobre ecología, podrían aumentar la capacidad para medir con precisión la magnitud del exceso de cáncer relacionado con la contaminación del aire.

Palabras clave: contaminación del aire; neoplasmas pulmonares/riesgo; revisión

(1) The Health Effects Institute, Cambridge, MA, United States of America (USA).

(2) Brigham Young University, Provo, UT, USA.

(3) The Channing Laboratory Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.

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Reprint requests to: Dr. Frank Speizer, Channing Laboratory, Harvard Medical School, 180 Longwood Avenue, 102115 Boston, Ma, USA.

An association of air pollution with lung cancer has been observed for at least 40 years.<sup>1</sup> This association, however, has received only sporadic attention because of the predominate role played by cigarette smoking in the vast majority of lung cancers in Western industrialized nations. Many scientists have taken the view that epidemiology could not reliably detect what must certainly be small relative increases against the high background rate due to etiologies involving cigarette smoking.<sup>2</sup> Nonetheless, even more recent epidemiologic studies, using improved analytic methods, suggest that ambient air pollution is a contributing risk factor for lung cancer. Moreover, despite some progress in reducing air pollution in many parts of the world, large numbers of people continue to be exposed to pollutant mixtures containing known or suspected carcinogens.

Ambient air, particularly in densely populated urban environments, contains a variety of known human carcinogens, including organic compounds such as benzo [a] pyrene and benzene, inorganic compounds such as arsenic and chromium, and radionuclides.<sup>3</sup> These substances are present as components of complex mixtures, which may include carbon-based particles, to which the organic compounds are adsorbed, oxidants such as ozone, and sulfuric acid in aerosol form. The combustion of fossil fuels for power generation or transportation is the source of most of the organic and inorganic compounds, oxidants, and acids, and contributes heavily to particulate air pollution in most urban settings. The radionuclides result from fuel combustion as well as from mining operations.

Since the mid-1980s there has been an increase in the number of epidemiologic studies that report health effects associated with particulate air pollution. Health effects have been observed at levels common to many urban areas. Although the biological mechanisms involved are poorly understood, recent epidemiological evidence suggests that respirable particulate air pollution is a risk factor for respiratory morbidity and cardio-pulmonary mortality. Acute and long-term exposure to elevated levels of particulate air pollution has been associated with a wide range of acute and chronic nonmalignant respiratory health endpoints including: a) declines in lung function; b) increased incidence and duration of respiratory symptoms; c) exacerbation of asthma; d) restricted activity; e) increased hospitalization for respiratory disease; and f) increased cardio-pulmonary mortality.<sup>4,5</sup> These findings suggest that combustion-source particulate air pollution is a pulmonary toxicant that can adversely affect the respiratory system in a variety of ways.

Experimental toxicology studies have documented the mutagenic and carcinogenic properties of combustion-source air pollution, such as diesel exhaust which is common in urban and highway environments.<sup>6</sup> Several lines of epidemiologic evidence also suggest that exposure to outdoor air pollution is associated with increases in the rate of lung cancer. In this chapter, we will review this evidence, focussing on studies of occupational groups, comparisons of urban and rural populations, between-community studies, and case-control and cohort studies, including three recent prospective cohort studies. In addition, the plausibility of ambient air pollution/lung cancer effect will be discussed by summarizing epidemiologic evidence of relative risks of various types of exposure to combustion-source pollutants.

### Occupational exposure

Lung cancer rates are increased among occupational groups exposed to combustion products of fossil fuels over a wide range of exposure. Studies of British coal gasification workers, reported some 30 years ago, observed excess risk of lung cancer among exposed workers.<sup>7</sup> Later, studies of US steel workers documented their exposure to high levels of coal combustion-related air pollution. These studies of coke-oven workers by Lloyd and colleagues<sup>8</sup> and Redmond *et al*<sup>9</sup> observed that increasingly greater excesses of lung cancer were associated with workers exposed to low, medium, and high exposures. There was also an increase in lung cancer associated with increased length of exposure (Table I). Relative risks of respiratory cancer ranged from approximately 2 to 16, depending on the level and length of exposure.

Various groups of workers occupationally exposed to diesel exhaust, such as railroad, bus garage, and dock workers and truckers, have been observed to be at in-

**Table I**  
**RELATIVE RISKS OF DEATH FROM RESPIRATORY**  
**CANCER (1953-1970) FOR COKE-OVEN WORKERS**  
**IN ALLEGHENY COUNTY, PA**

Level of exposure (work area)	Length of employment		
	5+ yrs	10+ yrs	15+ yrs
Low (side only)	1.79	1.99	2.00
Medium (part-time topside)	2.29	3.07	4.72
High (full-time topside)	9.19	11.79	15.72

Adapted from Redmond<sup>9</sup>

creased risk of lung cancer in multiple studies.<sup>10</sup> These studies have generally observed 40-50% increases in lung cancer risk that are not explained by known confounders such as cigarette smoking. Few studies, however, have collected information on actual levels of diesel exhaust in the work environment, complicating considerably their interpretation. For example, a recent case-control study of Teamster union members in the mid-Western US found excess lung cancer among mechanics and short- and long-haul truckers that could not be explained by known lung cancer risk factors such as cigarette smoking or diet. The lung cancer rate ratios for employment in various jobs were associated with present-day levels of elemental carbon, a relatively specific marker for diesel exhaust, measured in the repair shops, truck cabs, and in highway and residential environments (Table II).<sup>11</sup> The present day levels of elemental carbon in truck cabs were slightly higher on average than highway background, but on average 4 times greater than those in residential neighborhoods in the Midwest. However, recently assembled data suggest that between 1958 and 1981, Los Angeles residents may have been exposed to ambient air pollution levels as high or higher than those currently associated with truck driving.<sup>12</sup>

### Environmental exposure

Studies that contrast lung cancer rates between urban and rural environments generally have found evidence of increased lung cancer in urban dwellers (Table III).

**Table II**  
**LUNG CANCER RELATIVE RISK ESTIMATES**  
**FOR TEAMSTER JOB CATEGORIES**

Job category	Elemental carbon (g/m <sup>3</sup> )	Adjusted RR estimate
Unexposed	1.1-2.5	1.0
Truckers: Long haul	3.8	1.3
Truckers: City	4.0	1.3
Mechanics	12.0	1.7

Data from Steenland<sup>11</sup>

Although many of these studies attempted to control for cigarette smoking, Doll and Peto<sup>17</sup> have suggested that the remaining urban/rural difference may be due to urban dwellers having started smoking at younger ages as cigarette smoking became increasingly prevalent in the early 20th century. Moreover, cancer incidence data collected by IARC continue to show evidence of urban-rural differences in lung cancer rates with urban to rural rate ratios between 1.0-1.9.<sup>26</sup> Dean<sup>22</sup> controlled for age at beginning smoking and found that the urban/rural difference persisted. Furthermore, studies of population migration from high-exposure countries to lower-exposure countries suggest that migrants have lasting risk related to their country of origin and previous exposures.<sup>27-29</sup> However, urban/rural differences may reflect, at least in part, unaccounted for differences in smoking habits, occupational exposures, migration patterns, or other factors related to population density.

**Table III**  
**URBAN/RURAL DIFFERENCES IN LUNG CANCER**

Studies	Population	Cases	Rate ratio
Cohort studies			
Hammond and Horn <sup>13</sup>	US veterans (1952-1955)	448	1.3
Buell <i>et al.</i> <sup>14</sup>	California residents (1957-1962)	304	1.3
Hammond <sup>15</sup>	US residents (1959-1965), unexp./exp. to dust and fumes	1 510	1.1/1.3
Cederlof <i>et al.</i> <sup>16</sup>	Swedish men (1963-1972)	116	1.4
Doll and Peto <sup>17</sup>	British physicians (1951-1971)	401	1.0
Tenkanen and Teppo <sup>18</sup>	Finnish men (1964-1979), smokers/nonsmokers	233	1.1/1.9
Case-control studies			
Stocks and Campbell <sup>19</sup>	British men (1952-1954)	725	1.7
Haenszel <sup>20</sup>	US white men (1958)	2 381	1.4
Haenszel and Taeuber <sup>21</sup>	US white women (1958-1959)	749	1.3
Dean <sup>22</sup> <i>et al.</i> <sup>23</sup>	Irish men/women nonsmokers (1960-1962)	3 040	2.1/1.3
Hitosugi <sup>24</sup>	Japanese men/women (1960-1966)	259	1.8/1.2
Samet <i>et al.</i> <sup>25</sup>	New Mexico residents > 25 yrs in urban counties (1980-1982)	422	1.2-1.4

Several studies have compared lung cancer rates between areas with differing levels of air pollution (Table IV). Another study has evaluated trends in lung cancer mortality rates across different wards with differing levels of air pollution in the Tokyo metropolitan area.<sup>33</sup> These studies found evidence of relative excesses of lung cancer in the more polluted areas of similar or slightly higher magnitude than the urban/rural studies. However, incidence, exposure, and covariate data were all on the aggregate, or ecologic, level so interpretation of these results is complicated by several factors, including the inability to adequately account for individual and between area differences in other risk factors.<sup>34</sup>

Two studies took advantage of "natural experiments". Stevens and Moolgavkar<sup>35</sup> observed declines in lung cancer incidences among nonsmoking males in England and Wales coincident with substantial declines in levels of particulate and sulphur dioxide pollution that resulted from the implementation of nation-wide air pollution control measures. Observing that the rates of lung cancer began their decline within a few years of the reduction in air pollution, critics have challenged the authors' interpretation of the data. The authors countered that reductions in lung cancer risk in ex-smokers have been observed within two years of quitting smoking.<sup>35</sup>

In another study, Archer<sup>32</sup> analyzed respiratory cancer mortality in two Utah counties with very low smoking rates. These two counties were similar in many respects, with low and nearly equal respiratory cancer mortality rates until a steel mill constructed during WWII caused substantial increases in air pollution in one of the communities. The subsequent differences in lung cancer were substantial within about 15 years after the increase in air pollution and have persisted. A third neighboring county, unaffected by the steel mill's pollution, but with higher smoking rates had higher lung cancer rates than either of the other two counties—underscoring the profound effects of cigarette smoking on lung cancer risks.

**Table IV**  
**ECOLOGIC STUDIES OF AIR POLLUTION AND LUNG**  
**CANCER**

Study	Locale	Average PM <sub>10</sub> in high exposure region (g/m <sup>3</sup> )	Rate Ratio
Henderson <sup>30</sup>	Los Angeles	53-64	1.3
Buffler et al. <sup>31</sup>	Houston	41-46	1.9
Archer <sup>32</sup>	Utah	47-53	1.6

Most of these studies suffer from the lack of a direct measure of the air pollution burden experienced by the study population.

### Case-control and recent prospective cohort studies

Several case-control and cohort studies used air pollution monitoring data to estimate the exposures of study subjects (Table V). The case-control studies found relative increases of lung cancer risks after adjustment for age (all studies), smoking,<sup>37-41</sup> and occupational exposure<sup>36-38,40-41</sup> similar to those observed in the urban/rural and ecologic studies.

Three recent prospective cohort studies which made direct estimates of particulate air pollution have estimated the effect of air pollution exposure on lung cancer mortality. The study by Abbey et al<sup>42</sup> followed a cohort of Seventh Day Adventists. This cohort had extremely low prevalence of smoking and relatively uniform and healthy dietary patterns, which reduced the potential for important confounding by these factors. Excess lung cancer was observed in relation to both particle and ozone exposure.

Dockery and colleagues recently reported the results of a 14 to 16-year prospective follow-up of 8 111 adults living in six US cities<sup>43</sup> which evaluated associations between air pollution and mortality (Table V). Mortality was ascertained through 1989 and TSP, PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>4</sub>, H<sup>+</sup>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> levels were monitored. Mortality risk was estimated via Cox proportional hazards regression modeling while directly controlling for individual differences in age, sex, cigarette smoking, BMI, education, and occupational exposure.

The largest estimated mortality risk was associated with cigarette smoking. However, after controlling for individual differences in age, sex, cigarette smoking, BMI, education, and occupational exposure, differences in relative mortality risks across the six cities were strongly associated with differences in pollution levels in those cities. Associations between mortality risk and air pollution were strongest for respirable particles and sulfates. Air pollution was positively associated with lung cancer mortality and cardiopulmonary disease mortality—but not with mortality from other causes combined. After adjustment for the other risk factors, a 37% excess lung cancer risk was observed for a difference in fine particle pollution equal to that of the most polluted versus the least polluted city.

Another recent study evaluated particulate air pollution as a predictor of mortality in a prospective study of US adults.<sup>44</sup> This study linked ambient air pollution

**Table V**  
**CASE-CONTROL AND COHORT STUDIES OF AIR POLLUTION AND LUNG CANCER**

Study	Locale	Exposure classification	Rate ratio (95% CI)
<b>Case-control</b>			
Pike et al. <sup>36</sup>	Los Angeles	Residence in high pollution (Benz(a)pyrene) area	1.3 (NA)
Vena <sup>37</sup>	Buffalo, NY	>50 years residence in elevated TSP areas	1.7 (1.0-2.9)
Jedrychowski et al. <sup>38</sup>	Cracow	Residence in elevated TSP and SO <sub>2</sub> areas	1.5 (1.1-2.0)
Katsouyanni <sup>39</sup>	Athens	Lifelong residence in high pollution areas	1.1 (NA)
Barbone et al., <sup>40</sup> Biggeri et al. <sup>41</sup>	Trieste, Italy	Residence in high pollution areas	1.4 (1.1-1.8)
<b>Cohort</b>			
Abbey et al. <sup>42</sup>	California	PM <sub>10</sub> 42 d/yr > 100 g/m <sup>3</sup>	1.5 (0.9-2.4)
		O <sub>3</sub> 500 hr/yr > 100 ppb	2.3 (0.9-5.3)
Dockery et al. <sup>43</sup>	6 US Cities	Residence in high sulfate or fine particulate pollution areas	1.4 (0.8-2.3)
Pope et al. <sup>44</sup>	151 US Cities	Residence in high sulfate particulate pollution areas	1.4 (1.1-1.7)
Pope et al. <sup>44</sup>	151 US Cities	Residence in high fine particulate pollution areas <sup>a</sup>	1.0 (0.8-1.3)

<sup>a</sup> Data available for 50 of the 151 cities

data from 151 US metropolitan areas with risk factor data for 552 138 adults enrolled in the American Cancer Society (ACS) Cancer Prevention Study II (CPS-II). The study assessed vital status of participants from 1982 to 1989 using personal inquiries and automated linkage using the National Death Index. Data were analyzed using multivariate Cox proportional hazards regression modeling. The study controlled for individual differences in age, sex, race, cigarette smoking, pipe and cigar smoking, exposure to passive cigarette smoke, occupational exposure, education, body mass index, and alcohol use.

All-cause, and cardiopulmonary mortality, were consistently associated with sulfate and fine particulate pollution levels. Lung cancer mortality was associated with combustion source air pollution when sulfates were used as the index but not when fine particles was used as the index. To evaluate if this inconsistency was due to the use of different study areas or different pollution measures, sulfate pollution measures were included in models that were restricted to use data

only from the 47 metropolitan areas that had both sulfate and fine particulate measures. The results were similar to those from the initial analysis suggesting that the inconsistency was not due to differences in study areas, but lung cancer seems to be more strongly associated with sulfate particles than the more general index of fine particulate mass.

When sulfate particulate pollution was used as the index of exposure, estimated pollution-related mortality risk was as high for never smokers as it was for smokers and as high for women as it was for men. Although the increased risk associated with air pollution was small compared with that from cigarette smoking, results of this study suggest that the association between pollution and mortality was not likely due to inadequate control of smoking: a) the associations with air pollution persisted after controlling for cigarette smoking status, pipe and/or cigar smoking, years smoked and cigarettes smoked per day for both current and former smokers, and hours per day exposed to passive cigarette smoke; and b) associations were



as large for never smokers as they were for smokers. However, the small number of lung cancer deaths among nonsmokers, even in this large cohort, resulted in limited statistical power to observe lung cancer/air pollution effects in never smokers alone.

Potential interactions between ambient air pollution and other risk factors such as cigarette smoking remain largely unknown. Earlier reviewers have noted a greater than additive relation between air pollution and cigarette smoking suggesting both independent and joint effects.<sup>19,20,37,38</sup> Small numbers of nonsmoking lung cancer cases and the relatively small effect of air pollution compared to cigarette smoking results in imprecise estimates of joint effects.

### Plausibility of ambient air pollution/lung cancer effect

Combustion-source ambient air pollution has been associated with a wide range of nonmalignant health endpoints –suggesting toxic properties of this pollution– although the biological mechanisms involved are not well understood. Also, animal studies have documented mutagenic or carcinogenic activity for a wide range of combustion-source particles including those from the burning of tobacco, coal, diesel fuel, wood, and complex urban or industrial mixtures. Differences in the apparent magnitude of cancer risks associated with exposure to different combustion-source air pollutants are due, at least in part, to differences in relative toxic and carcinogenic activity of the pollutant. The level of lung exposure, or dose, also plays

an important role in determining the relative risk of various types of exposure.

Table VI summarizes epidemiologic evidence of relative risks of various types of exposure to combustion-source pollutants. The results suggest that breathing fine or respirable particles –from a wide variety of combustion sources– increases the risk of lung-cancer. The range of relative risk summarized in Table VI may be interpreted as not only reflecting the differences in relative carcinogenic activity of the pollutant, but also the level of exposure, or dose. Cigarette smoking represents the high end of combustion-source particle exposure; involuntary exposure to ambient air pollution and environmental tobacco smoke represents the low end of exposure.

The similar lung cancer risk estimates for environmental tobacco smoke and ambient air pollution may reflect similar differences in exposure. Spengler and colleagues<sup>45</sup> estimated that, on the average, a home with one smoker has concentrations of respirable particulate matter about 20 g/m<sup>3</sup> higher than homes without smokers. Similar or somewhat larger differentials in exposure exist between high and low polluted US cities. For comparison, in the Harvard Six Cities study, the range of PM<sub>10</sub> was 18 to 47 g/m<sup>3</sup> and the range of PM<sub>2.5</sub> was 11 to 30 g/m<sup>3</sup>. In the American Cancer Society, CPS-II study the range of PM<sub>2.5</sub> was 9 to 34 g/m<sup>3</sup>. Cigarette smoke has little impact on outdoor pollution concentrations. Outdoor combustion-source particulate air pollution penetrates indoors and, for persons from nonsmoking homes, the indoor, outdoor, and personal exposures are similar and highly correlated.<sup>46-48</sup> Estimated effects of ambient air pollution and envi-

**Table VI**  
**SUMMARY OF EPIDEMIOLOGIC EVIDENCE OF RELATIVE RISKS OF VARIOUS TYPES OF EXPOSURE TO COMBUSTION-SOURCE POLLUTANTS**

Exposed Groups	Primary combustion sources	Exposure indicators or indexes	Rate ratios
Cigarette smokers	Tobacco	Smoking status & history, cigarettes/day, etc.	7.0 - 22.0
Coke-oven workers	Coal	Job classifications	2.5 - 10.0
Railroad workers, truck drivers, diesel mechanics	Diesel	Job classifications	1.2 - 2.6
Residents of areas with high ambient air pollution	Complex mix from coal, wood, diesel, gasoline, etc.	Respirable, fine, or sulfate particle concentrations	1.0 - 1.6
Non-smokers exposed to environmental tobacco smoke	Tobacco	Smoking status of family members & co-workers, etc.	1.0 - 1.5

ronmental tobacco smoke can be viewed as at least partially complementary-both suggesting small lung cancer effects at relatively low levels of exposure to combustion-source air pollution.

### Estimates of population attributable risk

In the US, estimates of the population attributable risk of lung cancer due to air pollution have been published recently but they have used markedly different methods and their results span an order of magnitude (Table VII). For example, Doll and Peto<sup>17</sup> used estimates of benzo-[a]-pyrene in urban air and extrapolated from occupational studies of PAH-exposed workers. They estimated that less than 1% of future lung cancer would be due to air pollution from the burning of fossil fuels, although they noted that perhaps 10% of then current lung cancer in large cities might have been due to air pollution. In 1990 the US EPA estimated that 0.2% of all cancer, and probably less than 1% of lung cancer, could be attributed to the effects of air pollution.<sup>50</sup> This estimate was obtained by applying the unit risks for more than twenty known or suspected human carcinogens found in outdoor air to estimates of the ambient concentrations and numbers of persons potentially exposed. The unit risks were derived from either animal experiments or extrapolation from studies of workers exposed to higher concentrations. Karch and Schneiderman<sup>49</sup> using data from the American Cancer Society volunteers study and US Census data, estimated that the "urban factor" accounted for 12% of lung cancer in 1980. They predicted that 1980 levels of suspended particulates would be associated with a lung cancer rate ratio of 1.3, slightly less than the 47% increase observed for total suspended particles in the recent 6 Cities Study which reported on mortality

through 1989. Each of these estimates of attributable risk is subject to considerable error with respect to both the relative magnitude of effect and the proportion of the population assumed to be exposed, but there is no reason to prefer estimates based on extrapolation from animal experiments or occupational studies to direct observation of the populations at risk.

### Air pollution and lung cancer in less developed countries

As the foregoing discussion attests, current knowledge about ambient air pollution and lung cancer is based largely on the experience of populations of Western industrialized nations. The populations of the developing countries, however, are exposed to levels of air pollution from combustion sources in both ambient and indoor environments that rival or exceed those commonly observed in the industrialized West. Within the developing countries, the highest exposures, particularly among women, have been to indoor air pollution from the combustion of coal and biomass fuels for cooking and heating.<sup>51</sup> For example, typical concentrations of coal smoke in rural Chinese homes exceeded 500 g/m<sup>3</sup> and frequently exceeded 1 g/m<sup>3</sup>.<sup>51</sup> Smith<sup>52</sup> recently reviewed the epidemiologic literature on indoor air pollution and lung cancer in the developing countries and found consistent evidence of increased rates of lung cancer associated with indoor cooking and heating with coal in studies done largely in China. A much smaller group of studies revealed no consistent association of lung cancer with indoor use of biomass fuels.

There has been little research on ambient air pollution and lung cancer among urban residents of the burgeoning cities of the developing countries, although

**Table VII**  
**ESTIMATES OF THE POPULATION ATTRIBUTABLE RISK (PAR%) OF LUNG CANCER DUE TO AIR POLLUTION IN THE US POPULATION**

Source	Method	Estimated attributable risk
Doll and Peto <sup>17</sup>	Extrapolation from occupationally-exposed groups using past and then-current levels of BAP	0 - 2% overall (10% of current lung cancer in urban areas) 1% of future lung cancer
Karch and Schneiderman <sup>49</sup>	Relative risk of urban vs rural residents from Hammond and Garfinkel (1978) and proportion of 1980 population residing in urban areas	12% of 1980 lung cancer 10% - 19% of future lung cancer based on 1980 levels of TSP
US EPA <sup>50</sup>	Summation of numbers of cancers attributable to >20 individual pollutants from toxicologic and other data.	<1% given current levels of pollution



mounting levels of urban air pollution, from local stationary and, increasingly, mobile sources<sup>53</sup> is recognized as an important environmental problem by international public health and economic agencies. In the cities of the poorest developing countries WHO's Global Environmental Monitoring System observed average ambient concentrations of total suspended particles of 300 g/m<sup>3</sup>,<sup>51</sup> although levels in locales where coal is used for fuel, such as poor communities in South Africa, may exceed 1g/m<sup>3</sup>.<sup>54</sup> One might predict that the high levels of ambient air pollution found in cities in the developing world would be associated with greater excess lung cancer occurrence than has been observed in Western industrialized settings. Although there are currently few reliable data, a case-control study in Shenyang, China, observed 2-fold increases in lung cancer risk after adjustment for age, education, and smoking, among residents in "smoky" areas of the city and 1.5-fold increases among those in "somewhat or slightly smoky" areas.<sup>55</sup>

### Discussion of research needs

Direct epidemiologic observation of exposed populations can provide the best information for evaluating the magnitude of air pollution-related excess lung cancer if we can make more valid and precise estimates of air pollution exposure and the associated lung cancer risk. Clearly we need better data on both, particularly if we wish to make such estimates in the developing world.

While most studies have made some attempt to address confounding due to cigarette smoking and occupation, virtually none have addressed possible bias due to the measurement errors in exposure and covariates. Such bias, even if it is of equal magnitude among those with and without disease, can produce either spuriously high or low estimates of the lung cancer rate ratio in multivariable data. The problem is that few, if any, studies have collected the data necessary to quantify this bias, or often even to determine its likely direction. Future studies need to develop methods and collect data that can be used to quantify exposure measurement error and compute adjusted effect estimates.

Better estimates of the magnitude of effect will require large scale epidemiologic studies. Large numbers of cases will be necessary to measure the effects of air pollution and to measure joint effects of air pollution and factors such as occupation and smoking, and such studies will probably require pooling data from multiple locales. For such studies to be maximally in-

formative we will need to develop and apply improved epidemiologic methods. The development and application of new designs and statistical methods for air pollution studies should be supported. Navidi and Thomas<sup>56</sup> and Prentice and Sheppard<sup>57</sup> have described hybrid studies which combine ecologic-level contrasts of air pollution effects between cities with individual-level data on covariates, combining the strengths of both ecologic and individual-level studies. Studies using these designs could contrast the effect on lung cancer of exposure to the pollutant mixtures of different cities while effectively controlling confounding by cigarette smoking, diet, or other factors, and adjusting for exposure measurement error.

Methods for the retrospective estimation of lifetime exposure to air pollutants need to be developed and tested, so that large case-control and retrospective cohort studies can be conducted. These methods could be based on combinations of time-activity data and data from national aerometric databases such as those maintained by the US EPA. This effort should include development of methods to characterize, quantify, and adjust for exposure measurement error. Current work on biologic markers of exposure to and molecular effects of PAHs represents one approach to improving the characterization and accuracy of exposure estimation at the level of the individual.

The air pollution mixtures in major population centers should be characterized both in terms of physical and chemical constituents and in terms of sources of major constituents. If possible, retrospective characterization of levels of certain constituents could be accomplished.<sup>12</sup> This information would aid greatly in the interpretation of between city epidemiologic contrasts. For lung cancer epidemiology, urban and relatively clean areas with established population-based tumor registries should be targeted.

Finally, as a greater proportion of the world's population moves from rural communities to the rapidly expanding, and highly polluted, cities of Asia and the Southern Hemisphere, there is a clear need to address the large gap in epidemiologic research on air pollution and lung cancer in the developing world. These studies will present even greater challenges than those in the industrialized West. In addition to the generic problem of estimating long-term exposure to air pollution discussed above, the ambient air pollution mixture in urban centers in the developing countries is changing, due in part to the increase in automobile traffic. Characterizing these changes as they will have occurred over time, including choosing and measuring indicator pollutants for different pollution sources,

will require careful planning. In addition, the current tragic increases in cigarette smoking in the developing world,<sup>56</sup> and their thoroughly predictable consequences, will complicate the interpretation of studies of air pollution and lung cancer.

## Conclusions

The epidemiologic evidence indicates that ambient exposure to combustion-source air pollution is associated with small relative increases in lung cancer occurrence. These results are consistent with studies of other types of exposure to combustion-source pollution such as occupational exposures and exposures to environmental tobacco smoke. Relative to active cigarette smoking, the excess lung cancer risk associated with ambient air pollution is small. However, given the ubiquity of combustion-source ambient air pollution exposure, the contribution of this exposure across a population may be of public health importance. Errors in the measurement of air pollution exposure and in the measurement of other risk factors including cigarette smoking, continue to limit our ability to quantify the magnitude of the excess lung cancer risks associated with air pollution. Additional research that addresses these concerns, and that uses better estimates of exposure and more sophisticated analytic tools, is clearly warranted.

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